

**SOP#: RPS-12**

**NIH IRB Submission of Amendments**

**Version #: 2.2**

**Next Review Date: 05/2024**

**Approved Date: 05/2022**

**Review Interval Period: Biennial**

**NCI Clinical Director Signature:**

## **POLICY**

Any changes in research activities during the period for which IRB approval has already been given may not be implemented by Principal Investigators (PI) without prior IRB review and approval, except when necessary to eliminate apparent immediate hazards to the subject.

## **PURPOSE**

To identify the process in which a protocol amendment is submitted to the IRB for approval.

## **RESOURCES**

- NIH Office of Intramural Research Policies & Guidance [website](#)
  - Policy 106 - *Ancillary Reviews*
  - Policy 204 - *Levels of IRB Review and Criteria for IRB*
  - Policy 205 - *Requirements for IRB Submissions*
  - 400 Series - Regulatory Protections for Vulnerable Populations, as applicable
  - 500 Series - FDA Requirements for Human Subjects Research and Data and Safety Monitoring, as applicable
  - 700 Series - International Research Requirements, as applicable
- iRIS Helpful Documents [website](#)
- Institutional Review Board Office (IRBO) Ancillary Reviews [website](#)

## **PROCEDURES**

### **STEP 1: Prepare Revised Documents**

- Create a new amendment folder in the relevant protocol working folder on the PSO CCR Protocols Share Drive.

#### **Protocol**

- Retrieve the most recent approved version of the clean protocol. Note: If not clear from the working files, best practice would be to download the current, approved protocol from iRIS similar to the process for preparing a revised consent.
- Turn on track changes in Microsoft Word prior to making changes.
- Update the dates: Protocol title page and header, and/or Supplement.

- Make changes to protocol per PI instructions and/or outside Sponsor's amendment.
- Compare the protocol to the NIH/PSO protocol template and make updates as needed.
- Update Table of Contents in the protocol once all changes have been made.
- Save tracked versions of the protocol in the new amendment folder.
- If the amendment involves a:
  - Change in the accrual ceiling: create a revised Planned Enrollment Form and/or verify the new enrollment distribution with the PI. Note: This form does not need to be submitted but should be saved in the working file.
  - Change in dosimetry per RSC requirements: create a new or revised RSC Totals Worksheet/ICF Guide and update the protocol and consent per RSC template language.
  - Change in research blood volumes (or adding volumes for the first time): create a new or revised Blood Volume Calculator Tool and update the protocol and consent volumes, as needed.

### **Informed Consent**

- Download the approved consent(s) from iRIS, Word version.
- Turn on track changes in Microsoft Word prior to making changes.
- Update the first page in the consent(s) and the footer with the new version date.
- Make changes to document per PI instructions and/or outside Sponsor's amended consent.
- Compare the consent(s) to the NIH/PSO consent template and make updates as needed.
- Save tracked versions of the consent(s) in the new amendment folder.
- If the consent amendment involves a change in other sections from the protocol step above (e.g., blood volumes, dosimetry per RSC requirements) – update text accordingly.

### **Notification of Participants**

- If the Protocol and/or Consent amendment involves a change(s) that requires notification of participants, ask PI which participants will be notified and how they will be notified, e.g., verbally, via written letter, or re-consent with revised or new consent.
  - If participants will be notified verbally or via written letter, create a draft verbal script or participant letter to be used by the team.

### **Other/New Document(s)**

- If the amendment involves a new document submission and/or change(s) to another previously approved document, prepare the revised documents similar to above (e.g., tracked changes, updated version date, etc.).
- Save tracked versions of the new and/or revised document(s) in the new amendment folder.

**Note:** If the document being revised has a specialized document folder (e.g., Key Study Personnel [KSP]/Study Personnel Page [SPP]), save the document within that folder as well.

## **STEP 2: Create Cover Memo**

- The date on the cover memo should match the new version date on the protocol, NCI Supplement or Consent (if amendment is for consent changes only), or as on the revised document(s) if something else.
  - Note: When preparing and initially submitting multiple documents with the same amendment action, it is suggested to make all version dates consistent for initial submission, when possible. As documents are revised in response to pre-review corrections/stipulations, the dates will likely change/become different.
- Add a paragraph or two at the beginning of the memo to summarize the rationale and main purpose(s) of the amendment.
  - Include reference to the revised IB (if included with the amendment) in the summary, including rationale for changes based on the IB, safety updates or lack thereof, as applicable.
- List in detail all changes to the protocol, consent(s), and other documents (e.g., study personnel list [KSP]), as applicable, and provide a rationale for each change.
- Use the tracked version of each amended document to verify memo details.
- Save the cover memo in the new amendment folder.

## **STEP 3: Send Revised Documents to PI and Team for Review**

- Send all newly created documents, tracked revised documents and cover memo to the PI and research team for approval.
  - Save all correspondence with team regarding the amendment in a “correspondence” sub-folder of the amendment folder.
- Once approved by the PI/team, save the following in the protocol’s amendment folder:
  - Versions of any newly created documents for this amendment (e.g., verbal consent script/notification to participants).
  - Tracked versions of all previously approved/revised documents.
  - Any other relevant documents: revised IB, RSC approval (when applicable), etc., that may need to be attached to the Amendment Form.

## **STEP 4: Submit to Sponsor and/or Manufacturer (if applicable)**

- Submit protocol and consent amendments, as well as other documents, if applicable, to protocol Sponsor and/or Manufacturer for review and/or approval (as applicable per agreement terms)
  - Note: In most cases, this step must be completed before sending the Amendment to the IRB.

## **STEP 5: Submit for Scientific Review and other ancillary committees, if required**

- Submit the protocol amendment in iRIS to SRC for review if the amendment meets CCR amendment review requirements.

- Submit the protocol amendment to other ancillary committees (i.e., Radiation Safety Committee/RSC, Institutional Biosafety Committee/IBC, as needed).

#### **STEP 6: Initiate the iRIS Forms in preparation for QC and submission to IRB**

- Create a revision to the Study Application in iRIS and update it with any changes that correspond to the amendment, if applicable.
- Complete and submit Deputy Ethics Counselor (DEC) form if applicable.
- Create a new Amendment Form in iRIS and fill in any details that correspond to the amendment:
  - Select the type of changes relevant to the amendment
  - Check the KSP in iRIS to ensure KSP are listed correctly
    - Note: Check iRIS to ensure all KSP have current training.
  - Review that all relevant forms/documents needed for the amendment have been prepared for QC.

#### **STEP 7: Send Amendment for QC**

- Send the JIRA Task to PSO Director for QC.

Note: Do not attach any documents to the Amendment Submission Form in iRIS until after QC. Do not create clean versions of revised documents or pdf documents until after QC.

#### **STEP 8: Submit in iRIS**

- Finalize the Amendment Form in iRIS by checking/confirming the changes or incorporating any QC comments (as applicable).
- Attach the following documents to the Amendment Form:
  - Point by point Cover Memo (including the Sponsor and/or Manufacturer summary of changes, as applicable)
  - Study Application (if changes were made in the application)
  - Clean protocol and Supplement if applicable (if revised; MS Word Protocol or PDF version of combined NIH Supplement + Protocol)
  - Tracked protocol and Supplement if applicable (if revised; MS Word Protocol or MS Word Supplement and MS Word/PDF Protocol as separate documents)
  - Clean consent(s) (if revised; MS Word: clean – with black text if first time this consent is being submitted)
  - Tracked consent(s) (if revised; MS Word: tracked – with blue text if first time this consent is being submitted, otherwise text will already be black)
  - Study Personnel List (KSP) tracked and clean versions (if applicable)
  - SRC approval – CSO approval letter (if applicable)
  - DEC clearance (if applicable)
  - RSC approval (if applicable)

- Investigator's Brochure (if applicable)
- Any other revised documents, as applicable.

**Note:** Upload amendment documents in iRIS and "stack" all updated documents by checking out the older version and checking in again for proper stacking. Make sure to enter the document's new Version Date within the document attachment window.

- Route the Amendment Form for signatures
  - Assign for signature as indicated in iRIS.

### **STEP 9: Respond to Pre-Review Corrections and/or Stipulations (if applicable)**

- Move all documents associated with the initial amendment submission in iRIS to a new subfolder named "Initial Submission." The folder should be dated or numbered (e.g., "YYYYMMDD – Initial Submission" or "1. Initial Submission").
- Create another new subfolder in the protocol Amendment folder based on the type/timing of the review – e.g., "Response to IRB Pre-Review" or "Response to IRB Review/Stips" – as applicable. The subfolder should be dated or numbered (e.g., "YYYYMMDD – Response to IRB Pre-Review" or "1. Response to IRB Review/Stips" following the same convention chose in the prior bullet).
- Save the Pre-Review Correction iRIS Memo/Email or IRB Stipulation/Request for Correction Memo outcome letter in the subfolder for reference.
- Draft the reply and corrections to the required documents as applicable:
  - **Note:** Be sure to update the date of each document to be revised (i.e., both in the file itself as well as the file name with each response to pre-review corrections, post-review stipulations, etc.).
  - When responding to IRB Pre-Review comments: use the originally submitted tracked amendment documents and add any new changes.
  - When responding to IRB Stipulations (i.e., post-IRB review, not applicable if a review was deferred): use the clean versions of the submitted amendment documents (and track the new changes).
  - Contact PI/team to discuss any items that require their input and/or approval.
    - **Note:** Save relevant correspondence with PI regarding the amendment review/response input in the amendment sub-folder.
  - Incorporate any outstanding changes at this point (i.e., FDA requests, Sponsor changes) if applicable and **only if necessary** – if a reply to stipulations, IRB will need to send the response back to full board review if additional changes are made outside of those required by the stipulations.

**Note:** Response to stipulations must be submitted by the Due Date on the IRB Outcome Letter, if provided. Extensions can be granted in extenuating circumstances by emailing the NIH IRBO Analyst who processed the amendment.

- Enter the explanation of the changes for each stipulation/correction in the Review Response Submission Form in iRIS. Indicate section numbers where changes were made in the response text box as applicable.
  - Note: Consider adding a Word document to the Response folder where you draft replies to each of the Pre-Review Comments and/or IRB Stipulations for PI/team and QC feedback. If the changes are significant, submit for Sponsor/manufacturer review per their requirements.
- Review the final version of the revised/response document(s):
  - Review the tracked documents to ensure the changes have been made consistently.
  - Review the changes against the stipulations/corrections itemized in iRIS to ensure that all changes are documented, and the iRIS Study Application and Amendment Form have been updated as necessary.
  - Create final versions of the revised documents (clean and tracked), making sure to update Table of Contents (TOC) and pagination as needed.
- Upload/enter the response in iRIS and “stack” all updated documents in iRIS by creating a revision of each relevant submission document using the ‘create a revision’ function, as applicable. Make sure to enter the document’s new Version Date within the document attachment window.
- Assign for signature as indicated in iRIS.

#### **STEP 10: IRB Approval**

- The PI and Study Contacts will be notified of approval through iRIS Notification.
- Within the Amendment folder (or specialized document folder [e.g., KSP], as applicable), create an Approved Documents subfolder and save the following documents from iRIS:
  - IRB outcome letter(s)
  - Approved documents, as applicable:
    - Approved consent(s)
    - Final, clean version of the protocol
    - Cover Memo
    - Amendment Form
    - Review Response Submission Form(s) as applicable
    - Study Application (if changes were made in the application)
    - Other, as needed (e.g., KSP/SPP)
- Save the approved documents in the regulatory file.
- Forward copies of approved documents as needed (i.e., Sponsor, multi-center sites, etc.)
- Email IRB approval notification to PI and Study Coordinator with tracked change amendment documents as a notification of the approved protocol changes.
  - For CCR Sponsored studies, prepare protocol and/or consent with attached Cover Memo in eCTD format for submission to FDA per OSRO requirements.

- Within 3 days of IRB Approval, send JIRA Task to the IND Manager and request submission to FDA.

### **STEP 11: For Protocols with Foreign Language Long Form Consents**

Note: IRB Leadership agreed that for minor administrative changes to previously translated consent forms – translation may be done by a staff member who is fluent in the given language. The amendment request (i.e., Cover Memo) should indicate the name of the person who translated the document and the language they are fluent in. Any substantive changes will continue to require translation certification by a certified translator through the NIH Library or through an Institutes Translation contract.

- Submit an NIH Translations request [here](#) for any foreign language long form consent(s) once the IRB amendment approval has been received, if required.
  - Create a new sub-folder for Consent Translation in the specified Amendment folder and save any Correspondence regarding the translation in this folder.
- Once the translated long form consent(s) is/are received from NIH Translations or from the fluent staff member for administrative changes only, submit an Amendment Form in iRIS. Include the:
  - Cover Memo – indicate who provided the translation (i.e., official translation/certification of accuracy or by naming/identifying the qualified staff member who provided the translation, if applicable).
  - Translated long form consent(s) (clean version, and tracked versions as applicable)
    - **Note:** Ensure the consent version date matches the standard consent.
  - Translation Certification(s) of Accuracy, if applicable.
  - Complete the remainder of the Amendment Form.
- Assign for signature as indicated in iRIS.
- The PI and Study contacts will be notified of IRB consent approval (and translation certification of accuracy acknowledgement) through an iRIS notification from IRB.
- Within the Amendment subfolder for Approved Documents save the following documents from iRIS:
  - IRB outcome letter
  - Approved long form consent(s) as downloaded from iRIS
  - Translation Certification(s) of Accuracy, if applicable
  - Amendment Form
  - Study Application (if changes were made in the application)
- Save the approved documents in the regulatory file.